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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,540	10/07/2003	Frank H. Gaertner	DAS-103XC1	7752

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SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER

VOGEL, NANCY S

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/681,540	Applicant(s) GAERTNER ET AL.	
	Examiner Nancy T. Vogel	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 and 32-47 is/are pending in the application.
- 4a) Of the above claim(s) 11-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10, 19-41 is/are rejected.
- 7) ☒ Claim(s) 9 and 42-47 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) ☐ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) ☐ Notice of Informal Patent Application |
| 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) ☐ Other: _____ |

DETAILED ACTION

Claims 1-18, 32-47 are pending in the case.

Claims 11-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/10/06.

This application contains claims 11-18 are drawn to an invention nonelected with traverse in the response of 7/10/06. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 32-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 9/29/06, with claims drawn to ARCs made from *Pseudomonas fluorescens* withdrawn from the rejection. To recapitulate:

The rejection is based on the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, first paragraph "Written Description published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). Claim 1 is drawn to amended recombinant cells that comprise at least one heterologous gene encoding a chemokine or a cytokine. Dependent claims 2-8, 10 specify the particular chemokine or cytokine, including IFN-gamma,. Claim 41 specifies that the ARC contains an additional heterologous protein, and the identity of the heterologous protein. Claim 32 is drawn to a method of making ARC comprising introducing a gene encoding a chemokine or cytokine, growing and harvesting the cells, and inactivating or fixing the cells. Dependent claims 33-38 specify the type of cytokine or chemokine, including interferon-gamma, and the cell type. Claims 39 and 40 specify an additional heterologous protein in included. The specification has defined the term "ARC" as encompassing cells which 1) are dead; 2) have enhanced physical durability comprised to unamended living forms (resistance to disruption by sonic oscillation or French Pressure Cell; 3) are more susceptible to dissolution by proteolysis than their unamended living forms; and 4) contain recombinant heterologous genes and express heterologous proteins, wherein the desired function properties of the heterologous proteins are either partially or fully maintained (see page 8, para. 0080). Claims 1-8, 10 and 32-38 are genus claims in terms of cell type, since they encompass any type of cell

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(1-7, 10, 32-38), or any of gram positive or gram negative, yeast or fungi cells (8), treated with any type of agent which results in the properties listed above for ARCs. Claims 1, 2, 7, 8, and 10 are genus claims in terms of the recombinant protein produced, since any type of cytokine or chemokine (1, 8, 9, 10, 32) or any of a large list of chemokines or cytokines (2, 7, 33 and 38) are encompassed. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the methods of producing the claimed ARCs based on the teachings of the specification, i.e. killing the cell using conditions that result in maintenance of the activity of the recombinantly produced cytokine or chemokine, while also producing cells which are resistant to sonic or French Press disruption and sensitive to proteolysis. While the specification provides general information, including a large list of types of treatments which may be utilized, including acid, halogen, UV, phenols, anilides, hydroxyurea, quaternary alcohols, dyes, EDTA, organic and inorganic chemicals, aldehydes, psoralens, dessicating agents, etc. (page 9, para. 0031), the specification also states that the type of treatment will depend on the type of cell, the particular cytokine or chemokine, and the nature of the modification of the cellular structure required to produce cells having the stated properties of ARCs. There is no disclosure of types of treatments that would be useful for different types of cells, other than the one example provided, in which *P. fluorescens* that recombinantly expresses INF-gamma is treated with Lugol iodine. As disclosed by the specification, the treatment required for each different cell type and recombinant protein type may differ, and the specification does

not disclose any information regarding general rules for which type of treatment would be needed for any particular cell and protein. Further, the specification defines the product ARC cells by function only, and fails to describe the actual structures responsible for the properties that define the ARC cells. Therefore, the specification does not describe the claimed ARC cells and the method of producing said ARC cells in such full, clear, concise and exact terms so as to indicate that Applicant has possession of the method at the time of filing the present application. Thus, the written description requirement has not been satisfied.

Applicant's arguments, filed 1/29/07 have been considered but have not been found convincing.

Applicant has argued that as evidenced by the attached reference, "the scientific knowledge already in existence at the time the instant application was made would have indicated those agents that could confer the desired properties to cells within the scope of the instant claims. As indicated with McDonnell and Russell...mechanisms of action of a number of materials identified in the as-filed specification have been examined and a battery of techniques are available for studying the mechanisms of action in microorganism...Additionally, compounds capable of causing such effects were also reported in the literature ". However, it is maintained that while many agents capable of killing or fixing cells were known in the art, the specification does not provide sufficient description of which type of treatment would result in the claimed properties of ARC, i.e. treatments that result in the maintenance of the activity of the recombinantly produced cytokine or chemokine, while also producing

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cells which are resistant to sonic or French Press disruption and sensitive to proteolysis. Applicant argues in response to the rejections over Tarnowski and Steidler, that the disclosed treatment in these references do not result in the properties of the ARC cells. These references disclose treatments for fixing or inactivating microbial that are disclosed in the instant application as being possible treatments for the production of ARC cells, and yet according to applicant's arguments they do not give the desired results. Therefore, there is evidence that the application has not provided adequate description of the claimed cells having the properties of maintenance of the activity of the recombinantly produced protein, resistance to sonic or French Press disruption and sensitivity to proteolysis. While applicants may have provided a list of possible treatments that may result in the production of ARC cells as defined in the specification, this does not provide a sufficient written description since adequate written description requires more than a mere statement that a product is part of the invention, and reference to a potential method of isolating it. The product itself is required.

Therefore, only claims limited to *Pseudomonas fluorescens* derived ARC, and methods for making said *Pseudomonas fluorescens* derived ARC cells, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Tarnowski (US Patent 4,432,895).

This rejection is maintained essentially for the reasons set forth in the previous Office action, mailed 9/29/06.

Applicant's arguments filed 1/29/07 have been considered but have not been found convincing.

Applicant argues that since the reference discloses that the cells disclosed by Tarnowski et al. are disrupted by passage through a homogenizer and therefore "appear to be easily disrupted" (page 15). However, it is maintained that there is no disclosure in the reference of whether the level of resistance of the disclosed treated cells have is increased, decreased, or is the same, as the untreated cells. However, since as was previously argued in the rejection of 9/29/06, treatment by acid as was used in the reference, is one possible treatment listed as resulting in an ARC type cell. Furthermore, applicant argues that the cells disclosed by Tarnowski et al. contain interferon in an oligomeric form, which applicants state may be inactive or may have lower activity. However, there is no requirement in the specification or in the claims that the heterologous polypeptide need have any particular level of activity. Furthermore, any disclosure by Tarnowski that the interferon should be purified before use does not

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affect the teaching therein of the cells which meet the limitations of the claims, under 35 USC 102(b).

Claims 1, 2, 8, 10, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Steidler et al. (Infect. and Immun., Vol 66, No. 7, pp. 3183-3189, cited by applicants).

This rejection is maintained essentially for the reasons set forth in the previous Office action, mailed 9/29/06.

Applicant's arguments filed 1/29/07 have been considered but have not been found convincing.

Applicant has argued that Steidler et al. disclose that the cells comprising a cytokine (IL-2 or IL-6), and which are killed by mitomycin-C, do not meet the limitations of the claims since "[t]he reference teaches that treatment of the bacterial cells with mitomycin C abrogated the immunostimulatory effect of the IL-2 or IL-6 and that live cytokine secreting strains of bacteria were required to cause the desired biological effects (see Abstract, lines 8-10, page 2187; "Influence of lactococcal cell viability on immune responses elicited by recombinant *L. lactis*", page 3187, column 1 ; and Figure 6). Thus, it is respectfully submitted that the inactivated cells of Steidler et al. do not provide an active form of the cytokine when the cells were treated with the antibiotic and the reference does not anticipate the claimed invention. ". However, it is maintained that Steidler et al. do not in fact disclose that the cytokine proteins present in the mitomycin-C killed cells are inactive; rather, they disclose that administration of said

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cells to an animal does not result in the same effect as administration of live cells comprising said cytokine. They speculate that the difference could be attributed to the secretion of IL-2 or IL-6 by the live cells (see abstract). There is not disclosure in the reference stating that the mitomycin-C treated cells contain inactive IL-2 or IL-6.

Therefore, the rejection is maintained.

Claims 9 and 42-47 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

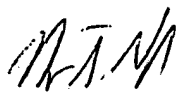
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NV
4/9/07


NANCY VOGEL
PRIMARY EXAMINER